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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 404

Application Number: 08/813,950
Filing Date: March 03, 1997
Appellants: ASSMUS ET AL.

Harris A. Pitlick
For Appellants

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 24, 2004.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief. Appeal No. 2000-1405 decided October 25, 2002 was an affirmation of the rejection of claims of instant application no. 08/813,950. The claims were directed to the same subject matter except the thermoplastic coating and binding agent was characterized as "a non-homogeneous mixture" and component B) was more broadly defined as from 95-5 wt.% of a flow improver.

The instant claims require the mixture to have a glass transition temperature of no more than 20°K below that of component A which is not required in the claims of the former appeal.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that claims 25-28 and claim 29 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Petereit et al., "Fast Disintegrating Controlled Release Tablets from Coated Particles," Drugs Made in Germany, volume 37, no. 2 (1994), pp. 1-8.

5,707,646	YAJIMA et al.	1-1998
5,603,957	BURGUIERE et al.	2-1997
5,552,159	MUELLER et al.	9-1996
5,858,412	STANIFORTH et al.	1-1999
51-91717	MEIJI SEIKA CO.	8-1976
5,484,608	RUDNIC et al.	1-1996
5,695,784	POLLINGER et al.	12-1997

(10) Grounds of Rejection

The following grounds of rejection are applicable to the appealed claims.

The text of section 103(a) of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the Drugs Made in Germany article by Petereit et al.

1. Petereit et al. shows a medicinal composition comprising a pharmaceutical active substance (page 2, first column, section 2.1.1, "Drug particles"), a thermoplastic coating of Eudragit RS 100 (page 2, section 2.1.3, "Film formers", lines 10-13, deemed to be a suitable species of thermoplastic acrylic plastic according to page 11, line 8 and page 20, Examples 1 and 2) and from 25-50% (page 1, Summary, lines 7-8) of an excipient such as glyceryl monostearate (page 2, section 2.1.2, "Excipients", second column, lines 9-10). The drug particles are coated in a fluid bed device (page 2, second column, section 2.2.1, "Taste masked preparations", lines 1-2) which indicates the flowing of a melt mixture of Eudragit acrylic polymer and glycerol monostearate through the drug particles to coat them.

2. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the Eudragit RS 100 acrylic polymer of Petereit et al. based on its acknowledged suitability in the instant specification.

3. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art composition predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in the reference and claims.

4. The claims are directed to an oral or medicinal composition prepared by hot-melt liquid application at a temperature of from 100-150°C and cooling which is a product-by-process claim. According to MPEP § 2113, the section entitled "Once a Product Appearing to be Substantially Identical is Found and a 35 U.S.C. 102/103 Rejection Made, the Burden Shifts to the Applicant to Show an Unobvious Difference":

> "If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process (*In re Thorpe*, 227 USPQ 964, 966, Federal Circuit 1985 and MPEP § 2113, the "Product-by-Process Claims' section)." "Once the examiner provides a rationale tending to show that the claimed product appears to be the same or similar to that of the prior art, although produced by a different process, the burden shifts to applicant to come forward with evidence establishing an unobvious difference between the claimed product and the prior art product (*In re Marosi*, 218 USPQ 289, 292, Federal Circuit 1983) and MPEP § 2113, the section entitled 'Once a Product Appearing to be Substantially Identical is Found and a 35 U.S.C. 102/103 Rejection Made, the Burden Shifts to the Applicant to Show an Unobvious Difference')."

5. The coating of Petereit et al. prepared from Eudragit RS 100 and from 25-50% of glycerol monostearate are the same species of thermoplastic acrylic plastic and the same glycerol monostearate in an equivalent concentration. Accordingly, the claimed product appears to be the same or similar to that of the prior art, shifting the burden to appellants to establish an unobvious difference between the claimed and prior art products. There is no evidence of record distinguishing the claimed method of coating over the fluid bed technique employed in Petereit et al.

Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yajima et al.

6. Yajima et al. (col. 5, Example 7 ; col. 6, Example 7 and col. 7, Example 13) shows a medicinal composition (col. 2, lines 45-51) containing a complex formed from 1-90% by weight (col. 2, lines 57-58) of a drug, from 1-60% by weight (col. 3, lines 7-8) of a functional polymer such as Eudragit E (deemed to be a suitable species according to page 11, line 8 of the instant specification) and a low melting point substance such as glycerol monostearate. The composition is produced by applying the Eudragit E polymer and glycerol monostearate in a hot-melt liquid state at 100°C followed by spray cooling.

7. The amount of glycerol monostearate ranges from the minimum amount required to dissolve or disperse the functional polymer (col. 2, lines 9-12) to 98% by weight (100% by weight of all components in the complex – 1% drug – 1% of functional polymer = 98% by weight).

8. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the Eudragit E functional polymer of Yajima et al. based on its acknowledged suitability in the instant specification.

9. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art composition predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in the reference and claims.

Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burguiere et al. in view of Mueller et al.

10. Burguiere et al. sets forth a medicinal composition obtained from a pharmaceutical active substance and a thermoplastic coating of from 60-85% by weight (col. 6, line 56) of Eudragit RL and/or RS (col. 6, line 11, acknowledged on page 11, line 8 of the instant specification) and as much as 20% by weight (col. 5, line 60) of a plasticizer such as glycerol monostearate (col. 6, line 35).

11. The claimed proportion of glycerol monostearate B) is "based on 100% by weight of A [thermoplastic acrylic plastic] and B." The maximum content of glycerol monostearate based on 100% by weight of Eudragit RL and/or RS and glycerol monostearate is 33.3% by weight which meets the limitations of claims 25 and 29.

12. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the Eudragit RL and/or RS of Burguiere et al. based on its acknowledged suitability in the instant specification.

13. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art composition predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in the reference and claims.

14. The claimed product prepared by a hot-melt liquid application process appears to be the same or similar to that of the prior art, shifting the burden to appellants to establish an unobvious difference between the claimed and prior art products. There is no evidence of record distinguishing the claimed method of coating over the organic solvent-based spraying procedure employed in Burguiere et al. (col. 7, lines 3-6).

15. Even if the hot-melt liquid application process of the claims is given weight, Mueller et al. recognizes the formulation of a medicinal composition by the hot-melt extrusion at a temperature of preferably from 60-150°C (col. 3, lines 16-19) of a pharmaceutical active substance with a polymer melt of an ethyl acrylate/methyl methacrylate/trimethylaminoethyl methacrylate chloride copolymer designated as Eudragit RL (col. 2, lines 46-47 and col. 4, Example 3) and as much as 30% by weight (col. 2, lines 11-12) of a conventional pharmaceutical auxiliary such as a wetting agent or plasticizer (col. 3, lines 5 and 6).

16. Mueller et al. (col. 1, lines 36-46) teaches:

> "The advantages of extrusion over other techniques such as granulation and tabletting is that the technology is simple, solvents are avoided, the number and amount of auxiliaries is minimized, it is possible to prepare fixed solutions, elaborate mixing processes are avoided and, in particular, the possibility of demixing of the components is avoided, in other words the composition of the individual depot forms throughout production is reliably absolutely constant. In addition there are the advantages of a continuous process with high throughput and small material losses."

17. It would have been obvious to prepare the medicinal composition of Burguiere et al. via the process of Mueller et al. to take advantage of the aforementioned features.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Staniforth et al. in view of Mueller et al.

18. Staniforth et al. (col. 5, lines 5-9) espouses a medicinal composition derived from a pharmaceutical active substance, an augmented microcrystalline cellulose, a sustained-release carrier such as an Eudragit RS or RL polymer (col. 20, line 30) and as much as about 20% by weight (col. 13, lines 37-40) of a surfactant such as glycerol monostearate (col. 11, line 33). Claim 29 is rescinded since the minimum amount of 33.3 wt% of glycerol monostearate is not recited.

19. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the Eudragit RS or RL polymer of Staniforth et al. based on its acknowledged suitability in the instant specification.

20. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art composition predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in the reference and claims.

21. The identical Eudragit RS or RL polymer and glycerol monostearate in an equivalent concentration to that claimed confirms that the claimed product appears to be the same or similar to that of the prior art. The burden is shifted to appellants to establish an unobvious difference between the claimed and prior art products. There is no evidence of record distinguishing the claimed method of coating over the fluidized bed manner described in Staniforth et al. (col. 21, lines 27-30).

22. Even if the product-by-process language is considered, it would have been obvious to formulate the medicinal composition of Staniforth et al. by the melt extrusion procedure of Mueller et al. in order to benefit from the attributes revealed in column 1, lines 36-46 of Mueller et al. presented hereinabove. Staniforth et al. is open to the application of the coating "in any pharmaceutically acceptable manner known to those skilled in the art (col. 21, lines 27-29)."

Claims 25-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Japanese Patent No. 51-91317, Rudnic et al. and Pollinger et al. in view of Petereit et al. and Mueller et al.

23. Burguiere et al. is no longer relied upon since both Rudnic et al. and Pollinger et al. disclose quantities of glycerol monostearate within the claimed parameters.

24. The Japanese patent is directed to a medicinal composition containing a pharmaceutical active substance and a thermoplastic coating of a 2-methyl-5-vinylpyridine/methyl methacrylate copolymer and a water-insoluble nonionic surfactant, particularly glycerol monostearate (translation, page 2, line 18).

25. The Japanese patent does not recite the claimed proportion of from 20-50 wt% of glycerol monostearate. Petereit et al. is described hereinabove and sets forth from 25-50% of excipients such as glycerol monostearate (page 1, Summary, lines 7-8 and page 2, paragraph 2.1.2, second column, lines 9-10). Petereit explains on page 7, second column, lines 5-10:

> "[A]n amount of less than 20% of excipients will result in a strong increase of initial dose, caused by damage of coatings on the particles [4]. Obviously the amount of excipient must be so high that a separating layer is formed also around the surfaces of the coated particles to prevent adhesion or even confluence of the coatings."

26. It would have been obvious to use the glycerol monostearate of the Japanese patent in the amount of from 25-50% espoused in Petereit et al. in order to form a separating layer around the "surfaces of the coated particles to prevent adhesion or even confluence of the coatings."

27. Rudnic et al. discusses a medicinal composition (col. 2, lines 43-49) obtained from a pharmaceutical active substance, an Eudragit RL, RS or E polymer (col. 2, line 57)and a hydrophobic or lipophilic matrix such as glycerol monostearate (col. 2, lines 63-64) or ATMUL 84S (col. 2, line 67) present in an amount of as much as 20.0% by weight (col. 4, Example 1, ATMUL 84S).

28. Pollinger et al. is drawn to a medicinal composition (col. 4, lines 29-30) yielded from a pharmaceutical active substance, Eudragit RL 30 D (col. 5, lines 3-4) and as much as 20% of a wetting agent such as glycerol monostearate (col. 6, lines 3 and 14). The coating is applicable "in customary coater equipment (col. 4, lines 60-61)."

29. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the polymers of Japanese patent, Rudnic et al. and Pollinger et al. based on its acknowledged suitability in the instant specification.

30. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art compositions predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in the references and claims.

31. The polymers and identical glycerol monostearate in an equivalent concentration to that claimed confirms that the claimed product appears to be the same or similar to that of the prior art. The burden is shifted to appellants to establish an unobvious difference between the claimed and prior art products. There is no evidence of record distinguishing the claimed method of coating over those described in the Japanese patent, Rudnic et al. and Pollinger et al.

32. Even if the product-by-process language is considered, it would have been obvious to formulate the medicinal composition of the Japanese patent, Rudnic et al. and Pollinger et al. by the melt extrusion procedure of Mueller et al. in order to benefit from the attributes revealed in column 1, lines 36-46 of Mueller et al. presented hereinabove.

Claims 25-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mueller et al. in view of Burguiere et al. and Petereit et al.

33. The references are described hereinabove. Mueller et al. is drawn to the formulation of a medicinal composition by the hot-melt extrusion at a temperature of preferably from 60-150°C (col. 3, lines 16-19) of a pharmaceutical active substance with a polymer melt of an ethyl acrylate/methyl methacrylate/trimethylaminoethyl methacrylate chloride copolymer designated as Eudragit RL (col. 2, lines 46-47 and col. 4, Example 3) and as much as 30% by weight (col. 2, lines 11-12) of a conventional pharmaceutical auxiliary such as a wetting agent or plasticizer (col. 3, lines 5 and 6). Claim 29 is rescinded since the minimum amount of 33.3 wt% of glycerol monostearate is not recited.

34. The claimed glycerol monostearate as the wetting agent or plasticizer is not recited. Burguiere et al. acknowledges the use of glycerol monostearate as a plasticizer (col. 6, lines 33-35) for medicinal compositions of a pharmaceutical active substance coated with Eudragit RL. Petereit et al. discloses glycerol monostearate as an excipient "to get fast disintegration of the tablets (page 1, Summary, lines 7-10)" and to form a separating layer around the coated particles "to prevent adhesion or even confluence of the coatings (page 7, second column, lines 7-10)."

35. It would have been obvious to utilize the glycerol monostearate of Burguiere et al. and Petereit et al. as the pharmaceutical auxiliary of Mueller et al. in order to enhance the flow properties of the coating which is an endemic function of plasticizers as indicated by Burguiere et al., or to form a separating layer around the coated particles to prevent adhesion or confluence of the coatings.

36. The claimed melting temperature, glass transition temperature (Tg) and melt viscosity at the melting temperature of the thermoplastic acrylic plastic A) is inherently possessed by the Eudragit RL copolymer of Mueller et al. based on its acknowledged suitability in the instant specification.

37. The claimed Tg of the mixture of at most 20°K below that of component A) is inherently exhibited by the prior art composition predicated on the identical types of thermoplastic acrylic plastic and glycerol monostearate utilized in Mueller et al. when considered in view of Burguiere et al. and Petereit et al. and claims.

(11) Response to Arguments

The arguments presented on pages 4-17 of the appeal brief is addressed *seriatum*.

First Assmus Declaration (filed 6/21/99)

38. The first Assmus declaration compares the homogeneity of mixtures prepared from Eudragit RS PO methyl methacrylate/ethyl acrylate/2-trimethyl-ammonium methacrylate chloride copolymer at different glycerol monostearate concentrations. The mixtures were melted at 60°C, 65°C and 80°C.

39. There is no comparison with a mixture representative of the claims wherein heating is conducted at a representative sampling of the claimed range of from 100-150°C to distinguish over the results reported in the table on page 2. The closest prior art with respect to the product-by-process hot-melt liquid application is Yajima et al. who exemplifies such a process at 100°C (col. 5, Example 4; col. 6, Example 7 and col. 7, Example 13) which is encompassed by the claimed parameters. The melting at 100°C was actually conducted and affirmatively exists. Accordingly, the heatings at 60°C, 65°C and 80°C do not reflect the closest prior art temperature of 100°C.

40. The evidence is not commensurate in scope with the claims regarding the broad scope of the claimed thermoplastic acrylic plastic A) which embraces myriad homopolymers and copolymers derived from structurally and functionally diverse monomers and comonomers according to page 8, line 22 to page 11, line 8 of the specification. The testing of a single quaternary ammonium-type acrylic copolymer does not confirm the criticality of the non-functional monomers or those containing hydroxyl, acid, tertiary amino, imidazoyl, piperazinyl, piperidyl, morpholino, and quaternary ammonium salts (page 8, line 14 to page 9, line 7 and page 10). There is no evidence of record that these diverse homopolymers and copolymers exhibit equivalent homogeneity to that of the tested quaternary ammonium-type acrylic copolymer. The quaternary ammonium-type acrylic copolymer has not even been tested at temperatures within the claimed limits to confirm its alleged homogeneity.

41. The results in the table on page 2 assigns ratings of from 1-4 based on descriptive degrees of inhomogeneity or homogeneity which could be a function of the evaluator. Such ratings are not empirically sound and cannot be scientifically verified in the absence of more objective means of determining homogeneity such as microphotographs.

Supplemental Assmus Declaration (filed October 15, 1999)

42. The Supplemental Assmus declaration compares blends of the same Eudragit RS PO quaternary ammonium-type acrylic copolymer with 50 wt.% of stearyl alcohol, stearic acid and polyethylene glycol (PEG 6000) and 50wt.% and 80 wt.% of glycerol monostearate when heated at 65°C, 100°C and 150°C.

43. The closest prior art product prepared by a hot-melt liquid coating process is the melt application at 100°C shown in Examples 4, 7 and 13 of Yajima et al. for thermoplastic coatings containing Eudragit E and glycerol monostearate. The tests involving stearyl alcohol, stearic acid and polyethylene glycol are of not germane to the closest prior art of Yajima et al. which actually uses the claimed glycerol monostearate. The examples tested at 65°C are not reflective of the closest prior art melt temperature of 100°C exemplified in Yajima et al.

44. The table on page 2 reports the identical homogeneity for stearyl alcohol, stearic acid and polyethylene glycol outside of the claims as that of the claimed glycerol monostearate. No distinction is seen between the claimed species of flow improver and the other tested kinds.

45. The homogeneity for an amount of glycerol monostearate at 50 wt.% within the claimed range yields is identical to that at 80 wt.% outside of the claimed maximum which is similar to the proportion employed in Examples 4, 7 and 13 of Yajima et al. (85.7 wt.%). Therefore, the claimed maximum level of glycerol monostearate of 50 wt.% is indistinguishable over that most resembling the closest prior art at 80 wt.%. A showing involving a single quantity at the claimed maximum of 50 wt.% is not commensurate in scope with the claimed range of as little as 20 wt.%.

46. The evidence is not commensurate in scope with the claims concerning a representative sampling of the innumerable species within the realm of the claimed thermoplastic acrylic plastic other than the exemplified Eudragit RS PO quaternary ammonium-type acrylic copolymer for the reasons of record set forth in paragraph 40 hereinabove.

47. The interactions between the flow improver and polymer of the photographs are rated by the symbols – indicating no interaction, + representing a change from rough to smooth of the polymer particle shape/surface (the beginning of interaction), and ++ reflecting very smooth (a strong interaction). It cannot be ascertained at what type of particle shape/surface the difference between no interaction and the beginning of interaction, as well as the difference between the change from rough to smooth to very smooth is qualified. Such subjective evaluations is predicated on the individual observer and cannot be scientifically validated in the absence of the photographs.

48. The Board of Patent Appeals and Interferences in the affirmation of the rejection in the instant application commented on the deficiencies of the Supplemental Assmus Declaration on page 10, line 9 to page 11 of the decision. Although the claims of the original appeal were directed to a wider range of component B) more broadly denoted as a flow improver, the concerns expressed therein remain pertinent to the instant claims.

49. The following deficiencies were noted:

a) "The appellants have not established that polymer particle smoothness correlates with melt homogeneity."

b) The evidence presented in the supplemental declaration is not commensurate in scope with the appellants' independent claim (*In re Grasselli*, 218 USPQ 769, 778, Fed. Cir. 1983 and *In re Clemens*, 206 USPQ 289, 296, CCPA 1980). Appellants' independent claim encompasses a great variety of thermoplastic acrylic plastics, yet only one thermoplastic acrylic polymer was used. "We find in the evidence of record no reasonable basis for concluding that the great number of materials encompassed by the appellants' claims would behave as a class in the same manner as the particular materials tested." (*In re Lindner*, 173 USPQ 356, 358, CCPA 1972 and *In re Susi*, 169 USPQ 423, 426, CCPA 1971).

50. The instant claims still broadly define the thermoplastic acrylic plastic A) and the lack of an established relationship between polymer particle smoothness and melt homogeneity clouds the comparisons in the table on page 2. Accordingly, the positions taken by the Board of Patent Appeals and Interferences in their affirmation of the rejection of the previously appealed claims remains applicable to the instant appeal.

51. Both of the declarations attempt to address the criticality of claimed product produced by the process of hot-melt liquid application of a coating comprising a thermoplastic acrylic plastic and glycerol monostearate to a medicinal composition at a temperature of from 100-150°C, followed by cooling. There is no evidence of record differentiating between the claimed hot-melt liquid application process and the coating processes of the other primary references such as the fluid bed technique of Petereit et al., the solvent-based spraying procedure of Burguiere et al., the melt extrusion of Staniforth et al., the liquid coating process of the Japanese patent, the dry mixing method of Rudnic et al. and the powder coating procedure of Pollinger et al.

Thus, appellants have not met the burden of establishing an unobvious difference between the claimed and prior art products predicated on their methods of manufacture which is the criteria for confirming the patentability of a product-by-process claim according to *In re Marosi*, 218 USPQ 289, 292, Fed. Cir. 1983. The declarations are not pertinent to Yajima et al. and Mueller et al. which show medicinal compositions produced by the claimed hot-melt liquid application at temperatures within the claimed parameters.

Re Petereit et al.

52. The teachings of a reference must be considered as a whole and are not confined to merely the examples. Petereit et al. (page 1, Summary, lines 7-8) sets forth from 25-50% of tabletting excipients. Glycerol monostearate is identified as a species of excipient (page 2, paragraph 2.1.2, second column, lines 9-10).

53. The statement on page 7, second column, lines 5-10 that at least 20% of excipients is required to prevent "strong increase of initial dose, caused by damage of coatings on the particles" and a high amount of excipient is desirable to prevent adhesion or confluence of the individual coated drug particles applies to all of the disclosed excipients. There is no disclosure that this statement is meant to specifically exclude glycerol monostearate.

54. Claim 29 is not separately patentable since Petereit et al. espouses from 25-50% of an excipient such as glycerol monostearate which embraces the claimed limits of from 33.3-50 wt.%.

Re Yajima et al.

55. Yajima et al. discloses a level of glycerol monostearate of from a minimum amount required to dissolve or disperse the Eudragit E polymer up to 98% by weight. There is no limitation as to the minimum level of glycerol monostearate necessary to solubilize the polymer. Examples 4, 7 and 13 show a ratio of glycerol monostearate to Eudragit E polymer of 6:1 for a complex containing 10% by weight of polymer. A complex containing the minimum 1% by weight of polymer would necessitate only 6% by weight of glycerol monostearate based on the 6:1 ratio exhibited predominantly throughout the examples of the patent.

56. Accordingly, a glycerol monostearate content of from 6% by weight up to 98% by weight of glycerol monostearate is within the ambit of Yajima et al. which encompasses the claimed range of from 20-50 wt.%. The consideration of the midrange values of the components in the complex reveals concentrations of 45% by weight of the drug, 30% by weight of the polymer and 25% by weight of glycerol monostearate. There is no evidence of record confirming the criticality of the claimed range over the closest prior art proportion shown in Examples 4, 7 and 13 of Yajima et al.

Re Burguiere et al. in view of Mueller et al.

57. Mueller et al. discloses the hot melt extrusion at 50-200°C, preferably from 60-150°C, of a pharmaceutical active substance, Eudragit RL polymer melt and as much as 30% by weight of a conventional pharmaceutical active auxiliary such as a wetting agent or plasticizer. The prior art melt extrusion is within the confines of the claimed hot-melt liquid application process. The primary reference to Burguiere et al. describes as much as 20% by weight of a glycerol monostearate plasticizer together with a Eudragit RS and/or RL polymer.

58. Mueller et al. is relied upon as a secondary reference to address the claimed product-by-process limitation. The secondary reference need not recite each and every element of the claims as long as it is sufficiently relevant to the teachings of the primary reference. The commonality of the references with respect to the disclosure of a medicinal composition comprising a pharmaceutical active substance, an Eudragit polymer and a plasticizer renders their combination proper.

59. Mueller et al. was utilized for the same reasons in the Board of Patent Appeals and Interferences affirmation mentioned hereinabove, albeit with different primary references due to the broader scope of component B). The Board found that the recitation in Mueller et al. of melt extrusion at 50-200°C is within the claimed hot-melt liquid application (decision, page 3, last paragraph; page 7, last paragraph and page 8, penultimate paragraph).

60. Claim 29 is not separately patentable since the proportion of 20% by weight of glycerol monostearate plasticizer of Burguiere et al. based on a composition containing 60% by weight of Eudragit RL and/or RS converts to 33.3% by weight predicated on 100% by weight of A and B as claimed.

Re Staniforth et al. in view of Mueller et al.

61. Staniforth et al. does not set forth "relatively large numbers of applicable combinations of ingredients." A sustained-release formulation comprising an active ingredient, an augmented microcrystalline cellulose, a sustained release carrier and a compressibility augmenting agent is espoused in column 5, lines 4-9 and column 6, lines 26-27. The sustained release carrier (col. 16, lines 50-58) includes a pharmaceutically acceptable acrylic polymer such as an aminoalkyl methacrylate polymer (col. 18, line 27). The compressibility augmenting agent includes a surfactant (col. 10, lines 32-34) such as glycerol monostearate (col. 11, line 33) in amounts of a large as 20% by weight (col. 13, lines 37-39).

62. Staniforth et al. clearly names Eudragit RS or RL as a sustained release carrier and glycerol monostearate surfactant as a compressibility augmenting agent. There is no evidence distinguishing the claimed broadly claimed composition, in particular the thermoplastic acrylic plastic, over that set forth in Staniforth et al.

63. Claim 29 is rescinded from this rejection since the minimum amount of 33.3 wt% of glycerol monostearate is not recited.

Re Japanese, Rudnic et al. and Pollinger et al. in view of. Petereit et al. and Mueller et al.

64. It is conceded that the Japanese patent does not recite the claimed quantity of glycerol monostearate. However, the Japanese patent considered in view of Petereit et al. renders obvious the employment of the glycerol monostearate in the amounts of from 25-50% taught by Petereit et al. in order to form a separating layer around the "surfaces of the coated particles to prevent adhesion or even confluence of the coatings (Petereit et al., page 7, second column, lines 5-10)."

65. Rudnic et al. sets forth a hydrophobic or lipophilic component such as glycerol monostearate without regard as to the concentration. The examples show levels of hydrophobic or lipophilic components of 5.0% and 20.0% by weight. One skilled in the art would surmise that the use of any of the hydrophobic or lipophilic components such as glycerol monostearate exhibits operability at 5.0% and 20.0% by weight. There is no statement that only certain species of hydrophobic or lipophilic components can only be incorporated at the specific exemplified amounts.

66. Even if the position is taken that Rudnic et al. does not recite the claimed content of glycerol monostearate, it would have been obvious to utilize the glycerol monostearate of Rudnic et al. at a proportion of from 25-50% set forth in Petereit et al. in order to form a separating layer around the "surfaces of the coated particles to prevent adhesion or even confluence of the coatings."

67. Pollinger et al. (col. 4, line 66 to col. 5, line 3) states that "[t]he compositions according to the invention, however, can only be prepared with microcapsules which are prepared using neutral methyl ester and/or ethyl ester compounds of polymethacrylic acid (®Eudragit NE 30 D, Rohm, Darmstadt) and/or quaternary ammonium compounds of polymethacrylic acid (®Eudragit RL 30 D, . . ." Eudragit RL 30 D is exemplified in column 13, lines 37-47. The disclosure of undersirable Eudragit E 12.5 polymer does not negate the positive teachings pertaining to Eudragit RL 30 D within the realm of the claimed thermoplastic acrylic plastic A).

68. Pollinger et al. (col. 6, lines 3 and 14) espouses as much as 20% of a wetting agent such as glycerol monostearate.

69. Bits and pieces have not been selected from the prior art. Each of the primary references disclose medicinal compositions containing a pharmaceutical active substance, a component embracing a Eudragit polymer, and a component encompassing glycerol monostearate. The burden of proof shifts to appellants to prove that the closest prior art formulations as represented by the examples do not yield unexpected results. Such a burden has not been met.

70. In response to the argument that an excessive number of references have been combined, reliance on a large number of references in a rejection does not, without more, weigh against the obviousness of the claimed invention.

(*In re Gorman*, 18 USPQ2d 1885, Fed. Cir. 1991).

Re Mueller et al. in view of Petereit et al. and Burguiere et al.

71. Although a plasticizer is not required in Mueller et al., as much as 30% by weight of a conventional pharmaceutical auxiliary such as a plasticizer or wetting agent is explicitly recited in column 2, lines 11-12 and column 3, lines 5 and 6. A component cannot be disregarded just because it is optional. It would have been obvious to formulate the medicinal composition of Mueller et al. with the glycerol monostearate

Burguiere et al. and Petereit et al. as the conventional pharmaceutical auxiliary of Mueller et al. in order to enhance the flow properties which is a function of plasticizers, or to prevent the adhesion or confluence of the coated particles.

72. Claim 29 is rescinded since the minimum amount of 33.3% by weight of glycerol monostearate is not recited.

73. It has been reiterated with respect to each of the rejections that the primary references do not recite the claimed Tg of the mixture of no more than 20°K below the Tg of component A). Each of the applied patents are directed to medicinal compositions containing a pharmaceutical active substance and a thermoplastic coating of an Eudragit polymer within the confines of claimed thermoplastic acrylic plastic A) and glycerol monostearate within the claimed proportion range. Based on the equivalent medicinal compositions of the prior art and claims comprising equivalent Eudragit polymers and the identical glycerol monostearate in equivalent amounts, the mixture of Eudragit polymer and glycerol monostearate of the references inherently possess a Tg of no more than 20°K below the Tg of the Eudragit polymer alone.

74. The original claims as well as the specification on page 5, line 13 to page 6, line 2 required the thermoplastic acrylic plastic A) combined with from 95-5 wt.% of a flow improver. Appellants originally found no distinction of the currently claimed glycerol monostearate in the narrower concentration range over flow improvers in general at wider proportion parameters. It is incumbent upon appellants to establish the criticality of the particular flow improver at a certain amount over the closest prior art glycerol monostearate proportions, or plasticizers or surfactants of the applied references. None the examples in the instant specification nor the declarations confirm the criticality of these limitations.

75. The claims are directed to a medicinal composition and not its method of preparation. Therefore, the language must be interpreted in light of the product (i.e. the medicinal composition) and not the hot-melt liquid application process. The products of Petereit et al., Yajima et al., Burguiere et al., Staniforth et al., Japanese Patent No. 51-91317, Rudnic et al., Pollinger et al. and Mueller et al. renders the claimed product obvious due to the common equivalent components of an Eudragit polymer and glycerol monostearate. Therefore, the product appears to be the same or similar to that of the prior art, shifting the burden to appellants to submit evidence of unobviousness. None of the examples in the specification nor the declarations indicate it for the reasons espoused hereinabove.

76. Even if the process language is given weight, the teaching in Mueller et al. of melt extrusion at 50-200°C addresses the claimed hot-melt liquid application as acknowledged by the Board of Appeal and Interferences in the affirmation.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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